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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,082	08/07/2001	Lawrence J. Marnett	11672N/0183US	1831

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STITES & HARBISON PLLC
401 COMMERCE STREET
SUITE 800
NASHVILLE, TN 37219

EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
12/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

richard.myers@stites.com
francine.vanaelst@stites.com

Office Action Summary	Application No.	Applicant(s)	
	09/924,082	MARNETT ET AL.	
	Examiner	Art Unit	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,9-43,49-59,61 and 62* is/are pending in the application.

4a) Of the above claim(s) *22-43 and 49-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7,9-21,55-59,61 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on August 31, 2009, amending claims 6 and 13, has been entered.

Claims 6-7, 9-43, 49-59 and 61-62 are pending. Claims 22-43 and 49-54 are withdrawn. Claims 6-7, 9-21, 55-59 and 61-62 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on August 31, 2009, have been fully considered and are not deemed to be persuasive to overcome the rejection previously applied.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-7, 9-21 and 55-62 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. in view of Tsujii et al.

Claims 6-7, 9-21 and 55-62 are drawn to a method of obtaining a sample from a living mammal, such as urine, contacting the sample with a solvent to extract an amount of PGH_2-EA metabolite in the sample, quantifying/measuring an amount of PGH_2-EA metabolites, relating the amount measure to the activity of the COX-2 enzyme and/or relating the amount of the metabolites to a disease state or progression of a disease state, such as cancer/tumor, by comparing the activity of the COX-2 enzyme in the mammal with a standard value of a previously detected/measured amount, or further generating a standard curve.

Yu et al. (Reference BN: PTO-1449) teaches a method of detecting/measuring COX-2 from a mammalian cell, by detecting/measuring a PGH2-EA metabolites (Figures 2-6 and pages 21182). Arachidonyl ethanolamide (AEA), a precursor for PGH_2-EA metabolites is not a substrate for COX-1 and therefore, the method of Yu et al. only selectively detects COX-2 activity (page 21182, right column, page 21183, right column, page 21184, right column and page 21186, left column). Yu et al. teaches a method of detecting/measuring COX-2 activity by detecting PGH2-EA metabolites via a mass chromatogram (Figures 3-5) and immunoassays (Figure 2 and Figure 6).

The difference between the reference of Yu et al. and the instant invention is that the reference of Yu et al. does not teach a method of detecting an activity of COX-2 enzyme in a living mammal by obtaining a sample from the living mammal and extracting PGH_2-EA metabolite from a sample using a solvent, the step of comparing the detected amount of PGH_2-EA metabolite to a previously determined amount from the mammal (standard value)/generating a standard curve, step of relating the amount of the metabolites to a disease state or progression of a disease state, such as cancer/tumor, or by obtaining an urine sample from a mammal by comparing the activity of the COX-2 enzyme in the subject with a standard value of a previously detected/measured amount.

However, since Yu et al. teaches a method of only selectively detecting COX-2 activity in a sample, one having ordinary skill in the art would have concluded to apply the teachings of Yu et al. in detecting COX-2 activity from a sample obtained from a living mammal. Further, it is well established and known in the art that COX-2 expression is increased in cancerous cells, such as in colon cancer cells, as disclosed by Taketo et al. (reference BK: form PTO-1449). With this knowledge in hand, one having ordinary skill in the art would have concluded to apply the teachings of Yu et al. to relate the amount of PGH2-EA metabolites and thereby COX-2 activity to disease state or progression of a disease state, such as colon cancer, by obtaining a sample from a mammal, such as an urine or blood sample, and by comparing the activity of the COX-2 enzyme in the subject with a standard value of a previously detected/measured amount or a standard curve.

Therefore, combining the teachings of Yu et al. and Taketo et al., it would have been obvious to one having ordinary skill in the art to apply the teachings of Yu et al. in following the progression of colon cancer or to monitor colon cancer in a subject by detecting COX-2 activity in a mammal by obtaining a urine sample from said mammal, extracting PGH_2-EA metabolite from a sample using a solvent, and detecting PGH_2-EA metabolites and comparing the detected amount of PGH_2-EA metabolite to a previously determined amount from the mammal (standard value)/generating a standard curve. One of ordinary skill in the art would have been motivated to combine the references in order to follow the progression or monitor colon cancer in a subject by detecting COX-2 activity by detecting PGH_2-EA metabolites. One of ordinary skill in the art would have had a reasonable expectation of success since Yu et al. successfully teaches selective detection/measurement of COX-2 activity in a sample and Taketo et al. teaches that COX-2 expression and thereby activity of COX-2 is increased in colon cancer cells in subjects.

Therefore, the above references render claims 6-7, 9-21 and 55-62 *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended in light of the amendment of the claims.

Applicants argue that the claims are not obvious over the cited references because Yu et al. induces COX-2, which is a clear distinction between taking a sample from a living subject and using that sample to determine COX-2 activity in the subject.

The rejection is not an anticipatory rejection, but an obviousness rejection. The crux of the claimed invention relies on the knowledge of specifically detecting COX-2 over COX-1 by measuring PGH_2-EA metabolites, since arachidonyl ethanolamide (AEA), a precursor for PGH_2-EA metabolites, is not a substrate for COX-1. The reference of Yu et al. is relied upon for said knowledge. MPEP 2144.01 states that "[I]n considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom." The disclosure of Yu et al. equips one having ordinary skill in the art to specifically detect/quantify COX-2 activity in a mammal in a non-invasive manner, by measuring/quantifying PGH_2-EA metabolites in a sample easily obtained from said mammal, such as from urine or blood, instead of administering to a mammalian subject a chemical that binds to COX-2 or a chemical that illicit an immunological response, which was the only option available to one having ordinary skill in the art (US Patent No. 6,045,773 and US Patent No. 5,459,239). Steps (a)-(e) are routine in the art, would have been obvious to one having ordinary skill in the art, and well within the means of one having ordinary skill in the art (see US Patent No. 5,686,269, US Patent No. 5,316,906, and US Paten No. 4,634,663).

Applicants refer to a “reverse Yu et al.”. It is not clear to the Examiner what applicants mean by "reverse of Yu et al.".

Applicants also argue that Yu et al. is heading the opposite direction of the present invention because instead of taking a sample and then determining the presence of COX-2 activity, Yu et al. induces COX-2 activity and then determines if said

induced COX-2 metabolizes AA and AEA. Examiner respectfully disagrees. Yu et al. does not teach away from the claimed invention. The crux of the reference of Yu et al. is that AA and AEA are metabolized by COX-2 but not COX-1. Therefore, it would have been obvious to one having ordinary skill in the art to apply the teachings of Yu et al. in determining COX-2 activity in a mammal (in following the progression of colon cancer or to monitor colon cancer in a subject) by obtaining a sample from said mammal and compare the amount of PGH_2-EA metabolites in said sample.

Applicants also argue that Yu et al.'s statement that "at the present time the physiological significance of the metabolism of AEA by COX-2 is not known." teaches away from invention because Yu et al. did not see a purpose for the metabolism of AEA by COX-2. It is not clear why such a statement would teach away from the claimed invention since the claimed invention is not drawn to a method of administering AEA, but measuring AEA metabolites.

Applicants also argue that there was no expectation of success. Examiner respectfully disagrees. MPEP 2143.02 states that "The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success The crux of the claimed invention relies on the knowledge of specifically detecting COX-2 over COX-1 by measuring PGH_2-EA metabolites, since arachidonyl ethanolamide (AEA), a precursor for PGH_2-EA metabolites, is not a substrate for COX-1. The reference of Yu et al. is relied upon for said knowledge. MPEP 2144.01 states that "[I]n considering the disclosure of a reference, it is proper to take into account not only specific teachings of the reference but also the inferences

which one skilled in the art would reasonably be expected to draw therefrom." one having ordinary skill in the art would have had a reasonable expectation of success since disclosure of Yu et al. equips one having ordinary skill in the art to specifically detect/quantify COX-2 activity in a mammal in a non-invasive manner, by measuring/quantifying PGH_2-EA metabolites in a sample easily obtained from said mammal, such as from urine or blood. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness by filing a declaration/affidavit under 37 CFR 1.132.

Applicants also argue that Taketo et al. fails to remedy the deficiencies of Yu et al. since Taketo et al. does not disclose or suggest the steps recited in the claims. Examiner respectfully disagrees. Steps (a)-(e) of claim 1 are routine in the art, would have been obvious to one having ordinary skill in the art, and well within the means of one having ordinary skill in the art (see US Patent No. 5,686,269, US Patent No. 5,316,906, and US Paten No. 4,634,663).

Hence the rejection is **maintained**.

Conclusion

None of the claims are in condition for allowance.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652